REMARKS

Claims 1-14, 29, 34, 35, and 38-58 are pending and are the subject of the instant office action.

A "clean" version of the now pending claims 1-14, 29, 34, 35, and 38-58 is shown above. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attachment is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE".

The rejections and objections set forth in the office action dated May 6, 2002 are addressed below.

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The undersigned wishes to clarify for the Examiner that it is intended that the fragment polypeptide recited in (c) of claim 40 does have Apo-2 ligand binding activity. Claim 40 has been amended, as shown herein, to clarify this property even further. The polypeptides embodied by (a) and (b) of claim 40 do not recite any specific functional limitation.

Claims 48 and 58 have been amended to correct the improper dependent form of the claims.

Claim 6 has been amended to clarify the language even further to more clearly identify the fragment referred to in (b) of claim 6.

Claims 1-6, 8-14, 29, 38-45, 47-55, 57 and 58 were rejected under Section 102(e) as being anticipated by Ni et al., US Patent 6,124,580. Applicants respectfully traverse this rejection for the reasons below.

The Ni et al. patent claims priority from US Provisional application no. 60/050,936 filed May 30, 1997 (the "first priority application") and US Provisional application no. 60/069,112 filed December 9, 1997 (the "second priority application"). Accordingly, the first priority application of Ni et al. was filed before the August 26, 1997 priority filing date of the instant application. However, the second priority application of Ni et al. was filed after the August 26, 1997 priority filing date of the instant application.

The Ni et al. patent discloses a polypeptide, referred to as TR10,

encoded by a cDNA cloned from a cDNA library. While the first priority application of Ni et al. discloses the cDNA sequence and deduced amino acid sequence of TR10, it fails to teach or suggest to one skilled in the art how to make and use the TR10 molecule. Example 4 in the Ni et al. first priority application (see pages 59-61 of first priority application) describes experimental results of certain Northern blot assays, but the data from those assays (e.g. that mRNA expression was found in multiple human normal and cancer cells and tissues) clearly does not provide sufficient disclosure as to the function of TR10. All of the remaining "examples" in the first priority application of Ni et al. are indeed prophetic, as can be seen from the fact that the examples are expressed throughout in the present tense.

The function, utility, and binding property(s) of the TR10 were solely postulated in the Ni et al. first priority application, based on sequence homology between the sequences of TR10 and other TNF receptor family members. Contrary to the Examiner's assertion, Ni et al. do NOT show binding of TR10 to Apo-2 ligand; that, too, is simply another prophetic guess on the part of Ni et al. As explained below, simply "guessing" in this receptor technology is not sufficient guidance to one skilled in the art. While as the Examiner notes in the Office Action that the Patent Laws do not mandate experimental testing, a prophetic teaching is only permitted where there is a reasonable expectation or reasonable prediction that the invention may be made and used in the way set forth by an Applicant. This receptor technology field is not reasonably predictable (absent any experimental characterization), and so a mere hypothesis on the part of Ni et al. does not suffice.

The TR10 molecule was not actually expressed or tested by Ni et al., and therefore its function or utility was not experimentally determined. In particular, Applicants wish to point out at least two factors why Ni et al. were <u>not</u> in a position to postulate function or utility of TR10 at the time of filing their first priority application. First, Ni et al. themselves teach in their specification that the "effects of TNF family ligands and receptors are varied and influence numerous functions, both normal and abnormal, in the biological processes of the mammalian system." (First priority application at page 5, lines 6-8; see also, page

34, lines 4-25). Such teachings clearly indicate that Ni et al. could not have reasonably predicted what function or activity TR10 may or may not have. Second, it is important to note the prophetic Example 5 provided on pages 62-63 of the first priority application. Example 5 teaches that TR10 will exhibit apoptotic activity. This speculative teaching is clearly wrong, as taught by Applicants' instant application, and by Ni et al.'s later filed application (as noted below).

It is therefore submitted that the first priority application of Ni et al. is not enabling for TR10 and does not satisfy the requirements of Section 112 or Section 101.

The Ni et al. second priority application was filed December 9, 1997, which is after the August 26, 1997 priority filing date of the instant application. It was not until the second priority application that Ni et al. experimentally found that TR10 bound Apo-2 ligand or inhibited apoptotic activity by Apo-2 ligand. As noted above, this finding is completely opposite of that reported by Ni et al. in Example 5 of the first priority application.[1] Accordingly, the Ni et al. patent is not entitled to its May 30, 1997 priority filing date for purposes of Section 102(e) against the instant claims.

A careful analysis of the disclosures of the first and second priority applications of Ni et al. clearly reveals (1) that the first application only disclosed TR10 in a non-enabling manner and (2) that a description of how TR10 could be used was not disclosed at all until after the priority filing date of the instant application.

For all these reasons, the Ni et al. patent does not have effective 102(e) prior art status against the present application and does not

[1]Compare the titles of Example 5 in the first priority application at page 62, "TR10 Induced Apoptosis", and that of Example 5 in the second priority application at page 41, "TR10 Inhibits TRAIL Induced Apoptosis."

anticipate the present claims. It is requested that the Section 102(e) rejection of the claims be withdrawn.

Respectfully submitted,
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please amend claim 6 to read as follows:

6. (Three times Amended) Isolated extracellular domain RTD polypeptide comprising (a) amino acid residues 56 to 212 of Fig. 1A (SEQ ID NO:1); or (b) a fragment of the sequence of [(a) which binds] amino acid residues 56 to 212 of Fig. 1A (SEQ ID NO:1), wherein said fragment binds Apo-2 ligand or inhibits Apo-2 ligand induced apoptosis in a mammalian cell.

Please amend claim 40 to read as follows:

40. (Twice Amended) Isolated nucleic acid comprising a polynucleotide encoding a polypeptide selected from the group consisting of:
a) a polypeptide comprising amino acid residues 1 to 386 of Fig. 1A (SEQ ID NO:1);
b) a polypeptide comprising amino acid residues 56 to 212 of Fig. 1A (SEQ ID NO:1); and
c) a fragment of the polypeptide of (a) or (b), wherein said fragment [which] binds Apo-2 ligand.

Please amend claim 48 to read as follows:

48. (Twice Amended) A process of producing RTD polypeptide comprising culturing the host cell of claim 44, wherein said nucleic acid comprised by said vector is expressed to produce [the] RTD polypeptide [of claim 1 or claim 6].

Please amend claim 58 to read as follows:

58. (Twice Amended) A process of producing RTD polypeptide comprising culturing the host cell of claim 54, wherein said nucleic acid comprised by said vector is expressed to produce [the] RTD polypeptide [of claim 40].